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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/756,411	01/08/2001	Franco Lori	NIH061.1CP1C2	5460

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[REDACTED] ART UNIT [REDACTED] PAPER NUMBER

1623

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/756,411	Applicant(s) Lori et al.
	Examiner L. E. Crane	Group Art Unit 1623

- THE MAILING DATE of this communication appears on the cover sheet beneath the correspondence address -

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE **--3--** MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be filed after six months from the date of this communication.
- If the prior for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty days will be considered timely.
- If NO period for reply is specified above, such period shall ,by default, expire SIX (6) MONTHS from the date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 USC §133).

Status

- Responsive to communication(s) filed on **-12/14/01 (amdt B)-**.
 This action is **FINAL**.
 Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- Claims **-9-19-** are pending in the application. Claims **-1-8 and 20-** have been cancelled.
 Of the above claim(s) **-1-** is/are withdrawn from consideration.
 Claim(s) **-1-** is/are allowed.
 Claims **-9-19-** are rejected.
 Claim(s) **-1-** is/are objected to.
 Claim(s) **-1-** are subject to restriction or election requirement.

Application Papers

- See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- The proposed drawing correction, filed on **-1-** are approved disapproved.
- The drawing(s) filed on **-1-** is/are objected to by the Examiner.
- The specification is objected to by the Examiner.
- The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119(a)-(d)

- Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119 (a)-(d).
- All Some * None of the CERTIFIED copies of the priority documents have been received.
- received in Application No. (Series Code/Serial Number) **-1-**.
- received in the national stage application from the International Bureau (PCT Rule 17.2(a)).
- * Certified copies not received: **-1-**.

Attachment(s)

- Information Disclosure Statement(s), PTO-1449, Paper No(s). **-1-**
- Notice of Reference(s) Cited, PTO-892
- Notice of Draftsperson's Patent Drawing Review, PTO-948
- Interview Summary, PTO-413
- Notice of Informal Patent Application, PTO-152
- Other: **-1-**

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Claims 1-8 and 20 have been cancelled, claims 16, 17 and 19 have been amended, and no new claims have been added as per the amendment filed December 14, 2001. The disclosure has been amended as requested.

5 Claims 9-19 remain in the case.

10 Claims 9-19 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

15 Claims 9-19 are directed to a compound, or to pairs of compounds, the chemical identity, or identities, of which either have not been specified or have been incompletely specified, and are therefore claimed far more broadly than is supportable by the instant disclosed exemplifications. In claims 16 and 19 in particular, the ingredient "ddC" has not been shown to be active against any retroviral infection including HIV in combination with hydroxyurea or a similarly active compound (See Table 7 at p. 26). In claim 17 the enablement of "AZT" as a active ingredient is questionable in view of the disclosures of the
20 Malley et al. patents (e.g. see abstract of 5,521,161, PTO-892 ref. E) which specifically exclude the combination of hydroxyurea and AZT as inactive against HIV in quiescent cells in culture.

Applicant's arguments filed December 14, 2001 have been fully considered but they are not persuasive.

25 Applicant argues that the newly provided reference "Balzarini" (PTO-892 ref. ZB) provides sufficient disclosure to enable the instant claimed

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subject matter for binary drug combinations other than hydroxyurea (HU) plus ddi, noting the specific disclosure that AZT and HU combinations were found to be active against HIV in activated cell culture. Applicant has missed the key inconsistency revealed by comparison of the Malley et al disclosures and the Lori et al disclosures; namely, are tests of anti-HIV activity made *in vitro* using quiescent cell cultures ala Malley et al. accurately predictive of anti-HIV activity *in vivo*, OR is the anti-HIV *in vitro* test regimen of Lori et al. accurately predictive of anti-HIV activity *in vivo*? Based on the factual basis for the claims in Malley et al '161 (PTO-892 ref. E) and the subsequent findings of Vila et al. (PTO-892 ref. XB), it appears to examiner that there is a valid correlation between *in vitro* and *in vivo* anti-HIV results in quiescent cell culture-based tests, BUT that there is not such a correlation with *in vivo* results when *in vitro* tests are conducted with activated cells in culture ala Lori et al. Therefore, the findings quoted in Balzarini (page 179, column 2, lines 15 et seq) to the effect that FddaraA plus HU is an effective treatment regimen for HIV is not believed by examiner because the test used to support this conclusion is a) done *in vitro* and b) done in the presence of activated cells (Lori test regimen), not the Malley et al regimen where a correlation between anti-HIV activity *in vitro* and *in vivo* has been established.

Examiner has reviewed pages 24-25 and Table 7 at page 26 and, because of the repeated use of terms like "expected," has come to the conclusion that the disclosure of Table 7 is entirely prospective for all combination therapies except that of hydroxyurea plus ddi, a finding of Malley et al. '161, PTO-892 ref. E. Therefore, applicant is respectfully requested to note *Ex parte Balzarini et al.* 21, USPQ 2d 1892, 1894 (BPAI, 1991) the first opinion of which stands for the proposition that claims directed to medicinal treatments of diseases in highly unpredictable art

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areas are properly rejected under 35 U.S.C. §112, first paragraph as lacking adequate enablement, in the absence of sufficient test data in support of the efficacy of the alleged treatment. See MPEP at 2107.03 (p. 2100-44, col. 2, in the August, 2001 revision).

5 Claims **9-10, 12-14 and 17-18** are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10 In claims **9 and 12-13**, the term “a compound that depletes ...;” in claim **9** the term “an antiviral nucleoside phosphate compound;” and in claims **12 and 13** the term “a second compound that ... inhibit(s) replication ... ;” are each directed to chemical compounds which have not been chemically identified thereby rendering the instant claims and some claims dependent therefrom both incomplete and lacking in properly defined metes and bounds. Applicant is respectfully requested to add by amendment specific, chemically identified, active ingredients in each of claims **9, 10, 12, 13 and 14** and particularly identify the species included within the generic terms “dideoxynucleoside” and “2'-fluoro purine dideoxynucleoside” in claims **17 and 18**, respectively.

20 Applicant's arguments filed December 14, 2001 have been fully considered but they are not persuasive.

25 Applicant has not responded to this grounds of rejection. Examiner notes that certain of the active ingredients in claims **16, 17 and 19** are now clearly identified. However, examiner also notes that applicant is apparently insisting on functional language in all of the remaining claims. This insistence suggests that applicant may have sufficient data to support extrapolation of Malley and Vila's findings to many other

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combination therapies, or alternatively theorizes that this is the case. Until data is provided to support this broad functional language, the instant grounds of rejection and the above rejection alleging lack of enablement will be maintained.

5 The non-statutory double patenting rejection, whether of the obviousness-type or non-obviousness-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornam*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir 1985); and *In re Goodman*, 29 USPQ 2d 2010 (Fed. Cir. 1993).

10 A timely filed terminal disclaimer in compliance with 37 C.F.R. § 1.321(b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R. §1.78(d).

15 Effective January 1, 1994, a registered attorney or agent or record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 C.F.R. §3.73(b).

20 Claims 9-17 and 19 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 12-22 of U.S. Patent No. 6,046,175. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are directed to a binary

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composition which includes two active ingredients generically defined in a manner which includes the subject matter previously claimed.

Applicant's arguments filed December 14, 2001 have been fully considered but they are not persuasive.

5 Applicant has acknowledged the appropriateness of the instant rejection has not provided an appropriate terminal disclaimer.

10 Claims 9-19 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 3-8 of U.S. Patent No. 6,194,390. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are directed to a method of treating HIV in a human host wherein the active ingredients are defined generically in a manner which includes the subject matter of the previously patented claims.

15 Applicant's arguments filed December 14, 2001 have been fully considered but they are not persuasive.

Applicant has acknowledged the appropriateness of the instant rejection has not provided an appropriate terminal disclaimer.

20 Claims 9-17 and 19 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 5,521,161. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are directed to a method of treating HIV in a human host wherein the active ingredients are defined generically in a manner which includes the subject matter of the previously patented claims.

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Applicant's arguments filed December 14, 2001 have been fully considered but they are not persuasive.

Applicant has acknowledged the appropriateness of the instant rejection has not provided an appropriate terminal disclaimer.

5 Claims 9-17 and 19 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 5,736,527. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are directed to a method of
10 treating HIV in a human host wherein the active ingredients are defined generically in a manner which includes the subject matter of the previously patented claims.

Applicant's arguments filed December 14, 2001 have been fully considered but they are not persuasive.

15 Applicant has acknowledged the appropriateness of the instant rejection has not provided an appropriate terminal disclaimer.

20 Claims 9-19 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 6-8 of U.S. Patent No. 6,093,702. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are directed to a binary composition which includes two active ingredients generically defined in a manner which includes the subject matter previously claimed.

25 Applicant's arguments with respect to claims 9-19 have been considered but are moot in view of the new grounds of rejection.

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Claims 9-19 of this application conflict with claims noted above in Patent Nos. 5,521,161, 5,736,527, 6,046,175, 6,093,702 and 6,194,390. 37 C.F.R. §1.78(b) provides that when two or more applications filed by the same applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one application. Applicant is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP §822.

10 Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL**. Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. §1.136(a).

15 A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. §1.136(a) will be calculated
20 from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

25 Papers related to this application may be submitted to Group 1600 via facsimile transmission(FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone numbers for the FAX machines operated by Group 1600 are (703) 308-4556 and 703-305-3592.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is **703-308-4639**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

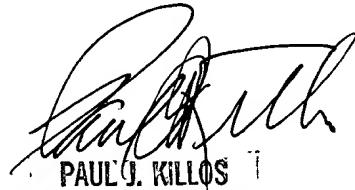
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Gary Geist, can be reached at (703)-308-1701.

10 Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is **703-308-1235**.

LECrane:lec
03/13/02



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PAUL J. KILLOS
PRIMARY EXAMINER